NDA 20-903/S004

Schering Corporation
Attention: Joseph F. Lamendola, Ph.D.
Vice President, U.S. Regulatory Affairs
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Dr. Lamendola:

Please refer to your supplemental new drug application dated September 1, 1999, received September 2, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Rebetol® (Ribavirin), 200mg capsules for use in combination with the previously licensed biologic product, Intron® A (interferon alfa-2b, recombinant), 3 million IU injectable.

We acknowledge receipt of your submissions dated September 1, 1999, March 2, 2000, May 15, 2000, May 17, 2000, and May 24, 2000.

This supplemental new drug application provides for revisions to the WARNINGS section of the REBETRON™ label, as follows:

> **Psychiatric**
> **Severe psychiatric adverse events, including depression, psychoses, aggressive behavior, hallucinations, violent behavior (suicidal ideation, suicidal attempts, suicides) and rare instances of homicidal ideation have occurred during combination Rebetol/Intron A therapy, both in patients with and without a previous psychiatric disorder.** Rebetol/Intron A therapy should be used with extreme caution in patients with a history of pre-existing psychiatric disorders, and all patients should be carefully monitored for evidence of depression and other psychiatric symptoms. Suspension of Rebetol/Intron A therapy should be considered if psychiatric intervention and/or dose reduction is unsuccessful in controlling psychiatric symptoms. In severe cases, therapy should be stopped immediately and psychiatric intervention sought. (See ADVERSE REACTIONS.)
>
> **Other**
> Fatal and non-fatal pancreatitis has been observed in patients treated with REBETOL/INTRON A therapy. REBETOL/INTRON A therapy should be suspended in patients with signs and symptoms of pancreatitis and discontinued in patients with confirmed pancreatitis.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted May 17, 2000). Accordingly, the supplemental application is approved effective on the date of this letter.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Destry M. Sillivan, M.S., Regulatory Project Manager, at (301) 827-2335.

Sincerely,

Debra Birnkrant M.D.
Acting Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research